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L19: Entry 25 of 68 File: USPT Jan 25, 2000

DOCUMENT-IDENTIFIER: US 6017734 A
TITLE: Unique nucleotide and amino acid sequence and uses thereof

Detailed Description Paragraph Right (331):
This example utilizes the ability to direct ODV to the target cell by incorporating receptors, fusion proteins etc. into the ODV envelope. Upon fusion with the host cell membrane the viral nucleocapsid is released into the host cell. When genes encoding therapeutic agents are genetically engineered into the viral genome under the control of promoters that are recognized by the host cell (i.e. baculovirus IE1 gene promoter), then this system can be utilized for gene delivery purposes. The obvious example uses gp120 and the AIDS virus. Engineering ODV to have a 23-CD4 receptor located on the viral envelope, enables the targeting of that virus directly to HIV infected cells. After membrane fusion with the HIV infected cell, a gene that is under the control of an appropriate promoter encoding an anti-HIV toxic protein could be delivered and expressed. The resultant protein production would mediate the killing of the HIV infected cell.

L7 ANSWER 5 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1991:182486 BIOSIS
DN BA91:97235
TI CHARACTERIZATION OF A CONSERVED T CELL EPITOPE IN **HIV**-1 GP41 RECOGNIZED BY **VACCINE**-INDUCED HUMAN CYTOLYTIC T CELLS.
AU HAMMOND S A; OBAH E; STANHOPE P; MONELL C R; STRAND M; ROBBINS F M; BIAS W
B; KARR R W; KOENIG S; SILICIANO R F
CS DEP. MED., JOHNS HOPKINS UNIV. SCH. MED., BALTIMORE, MD. 21205.
SO J IMMUNOL, (1991) 146 (5), 1470-1477.
CODEN: JOIMA3. ISSN: 0022-1767.
FS BA; OLD
LA English
AB A human CTL epitope located in a region of the **HIV**-1 envelope protein gp41 that is highly conserved among various **HIV**-1 strains was identified. This epitope was recognized by **CD4**+ CTL clones that were induced in seronegative humans by immunization with recombinant gp160. **Fusion proteins** carrying portions of the **HIV**-1 env gene and synthetic peptides were used to localize this epitope to amino acids 584-595 of the **HIV**-1 BRU env sequence. Only two positions within this epitope showed variation among North American **HIV**-1 isolates, and the substitutions were conservative in nature. The Lys to Arg substitution at position 593 abolished recognition, probably by interfering with the peptide-MHC interactins. This epitope was recogized in association with at least one subtype of the widely distributed human class II MHC specificity DPw4, namely DPw4.2. The relatively high frequency of this allel (27.2% among Caucasians) makes it likely that a larger fraction of the population would generate a response directed at this epitope than would be the case for epitopes recognized in the cortext of gene products of most other class II and class I loci. Interestingly, the closely related DP .beta.-chain allele types 4.1 and 2.1, which differ from 4.2 by 3 and 1 amino acids, respectively, were unable to present this gp41 peptide to DPw4.2-restricted clones. Comparison of the structure of this epitope with that of other peptides recongized in the context of DPw4.2 led to the identification of a consenses sequence for DPw4.2 binding peptides. Because the gp41 CTL epitope 584-595 identified here is highly conserved and is recognized in the cntext of a common DP allele, it may represent an important target region for **vaccine** development. Our results indicate that **vaccines** containing their epitope may induce in a significant fraction of those imunized CTL active against at least half of all **HIV**-1 strains.

L11 ANSWER 3 OF 3 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:38872 BIOSIS
DN PREV200000038872
TI Determinants of CD4 independence for a human immunodeficiency virus type 1
variant map outside regions required for coreceptor specificity.
AU LaBranche, Celia C. (1); Hoffman, Trevor L.; Romano, Josephine; Haggarty, Beth S.; Edwards, Terri G.; Matthews, Thomas J.; Doms, Robert W.; Hoxie, James A.
CS (1) Duke University Medical Center, LaSalle St. Ext., Durham, NC, 27710 USA
SO Journal of Virology, (Dec., 1999) Vol. 73, No. 12, pp. 10310-10319. ISSN: 0022-538X.
DT Article
LA English
SL English
AB Although infection by human immunodeficiency virus (**HIV**) typically requires an interaction between the viral envelope glycoprotein (Env), CD4, and a chemokine receptor, CD4-independent isolates of **HIV** and simian immunodeficiency virus have been described. The structural basis and underlying mechanisms for this phenotype are unknown.

We have derived a variant of **HIV**-1/IIIB, termed IIIBx, that acquired the ability to utilize CXCR4 without CD4. This virus infected CD4-negative T and B cells and fused with murine 3T3 cells that expressed human CXCR4 alone. A functional IIIBx env clone exhibited several mutations compared to the CD4-dependent HXBc2 env, including the striking loss of five glycosylation sites. By constructing env **chimeras** with HXBc2, the determinants for CD4 independence were shown to map outside the V1/V2 and V3 hypervariable loops, which determine chemokine receptor specificity, and at least partly within an area on the gp120 core that has been implicated in forming a conserved chemokine receptor binding site. We also identified a point mutation in the C4 domain that could render the IIIBx env clone completely CD4 dependent. Mutations in the transmembrane protein (TM) were also required for CD4 independence. Remarkably, when the V3 loop of a **CCR5**-tropic Env was substituted for the IIIBx Env, the resulting **chimera** was found to utilize **CCR5** but remained CD4 independent. These findings show that Env determinants for chemokine receptor specificity are distinct from those that mediate CD4-independent use of that receptor for cell fusion and provide functional evidence for multiple steps in the interaction of Env with chemokine receptors. Combined with our observation that the conserved chemokine receptor binding site on gp120 is more exposed on the IIIBx gp120 (T. L. Hoffman, C. C. LaBranche, W. Zhang, G. Canziani, J. Robinson, I. Chaiken, J. A. Hoxie, and R. W. Doms, Proc. Natl. Acad. Sci. USA 96:6359-6364, 1999), the findings from this study suggest novel approaches to derive and design Envs with exposed chemokine receptor binding sites for **vaccine** purposes.

L6 ANSWER 6 OF 16 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2000:38872 BIOSIS
DN PREV200000038872
TI Determinants of **CD4** independence for a human immunodeficiency virus type 1 variant map outside regions required for coreceptor specificity.
AU LaBranche, Celia C. (1); Hoffman, Trevor L.; Romano, Josephine; Haggarty, Beth S.; Edwards, Terri G.; Matthews, Thomas J.; Doms, Robert W.; Hoxie, James A.
CS (1) Duke University Medical Center, LaSalle St. Ext., Durham, NC, 27710 USA
SO Journal of Virology, (Dec., 1999) Vol. 73, No. 12, pp. 10310-10319. ISSN: 0022-538X.
DT Article
LA English
SL English
AB Although infection by human immunodeficiency virus (**HIV**) typically requires an interaction between the viral envelope glycoprotein (Env), **CD4**, and a chemokine receptor, **CD4**-independent isolates of **HIV** and simian immunodeficiency virus have been described. The structural basis and underlying mechanisms for this phenotype are unknown. We have derived a variant of **HIV**-1/IIIB, termed IIIBx, that acquired the ability to utilize CXCR4 without **CD4**. This virus infected **CD4**-negative T and B cells and fused with murine 3T3 cells that expressed human CXCR4 alone. A functional IIIBx env clone exhibited several mutations compared to the **CD4**-dependent HXBc2 env, including the striking loss of five glycosylation sites. By constructing env **chimeras** with HXBc2, the determinants for **CD4** independence were shown to map outside the V1/V2 and V3 hypervariable loops, which determine chemokine receptor specificity, and at least partly within an area on the gp120 core that has been implicated in forming a conserved chemokine receptor binding site. We also identified a point mutation in the C4 domain that could render the IIIBx env clone completely **CD4** dependent. Mutations in the transmembrane protein (TM) were also required for **CD4** independence. Remarkably, when the V3 loop of a CCR5-tropic Env was substituted for the IIIBx Env, the resulting **chimera** was found to utilize CCR5 but remained **CD4** independent. These findings show that Env determinants for chemokine receptor specificity are distinct from those that mediate **CD4**-independent use of that receptor for cell fusion and provide functional evidence for multiple steps in the interaction of Env with chemokine receptors. Combined with our observation that the conserved chemokine receptor binding site on gp120 is more exposed on the IIIBx gp120 (T. L. Hoffman, C. C. LaBranche, W. Zhang, G. Canziani, J. Robinson, I. Chaiken, J. A. Hoxie, and R. W. Doms, Proc. Natl. Acad. Sci. USA 96:6359-6364, 1999), the findings from this study suggest novel approaches to derive and design Envs with exposed chemokine receptor binding sites for **vaccine** purposes.

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L6 ANSWER 16 OF 16 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1995:108491 BIOSIS
DN PREV199598122791
TI Induction of antibodies to the human immunodeficiency virus type 1 by immunization of baboons with immunoglobulin molecules carrying the principal neutralizing determinant of the envelope protein.
AU Zaghouani, Habib; Anderson, Stephanie A.; Sperber, Kirk E.; Daian, Christina; Kennedy, Ronald C.; Mayer, Lloyd; Bona, Constantin A. (1)
CS (1) Dep. Microbiol., Mount Sinai Sch. Medicine, One Gustave Levy Place, New York, NY 10029 USA
SO Proceedings of the National Academy of Sciences of the United States of America, (1995) Vol. 92, No. 2, pp. 631-635.
ISSN: 0027-8424.
DT Article
LA English
AB The hypervariable region 3 (V-3) within the disulfide-bridged loop of the envelope protein of the human immunodeficiency virus type 1 (**HIV**-1) contains an amino acid sequence that was defined as a principal neutralizing determinant (PND). A 19-amino acid residue consensus sequence (designated V-3C) predicted from the PND sequences of 245 isolates as well as a sequence from the PND of the WMJ2 **HIV**-1 isolate (designated V-3M) were expressed on the variable region of murine-human immunoglobulin (Ig) **chimeras** that were designated Ig-V-3C and Ig-V-3M, respectively. The **HIV**-1 sequences on the Ig **chimeras** preserved their antigenicity and interacted with antibodies specific for peptides encompassing the V-3C and V-3M sequences. In baboons, Ig-V-3C and Ig-V-3M induced antibodies that bound V-3C and V-3M peptides as well as the glycoprotein gp120 envelope protein of **HIV**-1 MN isolate. In addition, the baboons' antisera were able to prevent infection of **CD4** SupT1 susceptible T cells by **HIV**-1 MN. Finally, Ig-V-3M **chimeras** were able to stimulate in vitro production of antibodies specific for the **HIV**-1 envelopederived peptides by lymphocytes from **HIV**-1-infected human subjects.

AN 1995:172497 BIOSIS
DN PREV199598186797
TI Immunogenic targeting of recombinant peptide **vaccines** to human antigen-presenting cells by chimeric anti-HLA-DR and anti-surface immunoglobulin D antibody Fab fragments in vitro.
AU Baier, Gottfried (1); Baier-Bitterlich, Gabriele; Looney, David J.; Altman, Amnon
CS (1) Inst. Med. Biol. Human Genetics, Univ. Innsbruck, Schoepfstr. 41, A-6020 Innsbruck Austria
SO Journal of Virology, (1995) Vol. 69, No. 4, pp. 2357-2365. ISSN: 0022-538X.
DT Article
LA English
AB To increase the inherently weak immunogenicity of synthetic peptide **vaccines**, we used recombinant DNA techniques to generate **chimeras** between immunogenic determinants of human immunodeficiency virus type 1 (**HIV**-1) gp120 and antibody Fab fragments reactive with surface structures displayed specifically on human antigen-presenting cells (APCs), including surface immunoglobulin D (sIgD) and class II major histocompatibility complex (MHC) molecules. Hybridomas producing anti-human MHC class II (HIA-DR) or surface immunoglobulin D monoclonal antibodies (MAbs) that recognize nonpolymorphic determinants were used to clone chimeric Fab gene fragments by employing an established procedure to generate antigen-binding Fab libraries in phagemid vector pComb3. Molecular and immunochemical analysis indicated that the expected chimeric Fab fragments expressing the **HIV**-1 epitopes were correctly cloned and expressed in Escherichia coli and retained the binding specificity of the native (hybridoma-derived) MAb. The chimeric Fab fragments targeted the linked **HIV**-1-derived antigenic determinants to the surface of human APCs in vitro, as evidenced by fluorescence-activated cell sorter analysis. Furthermore, such recombinant immunotargeted **HIV**-1 peptide antigens demonstrated improved immunogenicity over equivalent nonimmunotargeted control antigens, as shown by their ability to stimulate interleukin-2 production by **CD4**+ T-helper cells from human donors exposed to **HIV**-1 antigens. These data suggest that immunotargeting of recombinant peptide antigens via the attached Fab fragments facilitates uptake by human APCs with subsequent access to the MHC class II processing pathway thereby validating the immunotargeting concept for such recombinant subunit **vaccin**

L2 ANSWER 30 OF 100 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1999:397214 BIOSIS
DN PREV199900397214
TI Envelope-dependent restriction of human immunodeficiency virus type 1 spreading in **CD4**+ T lymphocytes: R5 but not X4 viruses replicate in the absence of T-cell receptor restimulation.
AU Vicenzi, Elisa (1); Bordignon, Paola Panina; Biswas, Priscilla; Brambilla, Andrea; Bovolenta, Chiara; Cota, Manuela; Sinigaglia, Francesco; Poli, Guido
CS (1) P2-P3 Laboratories, DIBIT, Via Olgettina 58, 20132, Milan Italy
SO Journal of Virology, (Sept., 1999) Vol. 73, No. 9, pp. 7515-7523. ISSN: 0022-538X.
DT Article
LA English
SL English
AB The human immunodeficiency virus (**HIV**) replicates in activated **CD4**+ T lymphocytes. However, only **CD4**+ Th2 and Th0, but not Th1, **CD4**+ T-cell clones have been reported to efficiently support **HIV**-1 replication. This dichotomous pattern was further investigated in the present study in Th1, Th2, or Th0 cell lines derived from umbilical human cord blood and in T-cell clones obtained from the peripheral blood mononuclear cells (PBMC) of healthy adults. Both primary and laboratory-adapted **HIV**-1 strains with CCR5 as the exclusive entry coreceptor (R5 viruses) efficiently replicated in Th1, Th2, and Th0 cells. In sharp contrast, CXCR4-dependent (X4) viruses poorly replicated in both polarized and unpolarized **CD4**+ T cells, including adults' PBMC infected several days after mitogenic stimulation. Unlike the X4 **HIV**-1NL4-3, a **chimera** in which the env gene had been replaced with that of the R5 **HIV**-1NL(AD8), efficiently replicated in both Th1 and Th2 cells. This X4-dependent restriction of **HIV** replication was not explained by either the absence of functional CXCR4 on the cell surface or by the inefficient viral entry and reverse transcription. T-cell receptor stimulation by anti-CD3 monoclonal antibodies fully rescued X4 **HIV**-1 replication in both Th1 and Th2 cells, whereas it did not alter the extent and kinetics of R5 **HIV**-1 spreading. Thus, R5 **HIVs** show a replicative advantage in comparison to X4 viruses in their ability to efficiently propagate among suboptimally activated T lymphocytes, regardless of their polarized or unpolarized functional profiles. This observation may help to explain the absolute predominance of R5 **HIVs** over X4 viruses

L2 ANSWER 12 OF 100 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:363571 BIOSIS
DN PREV200100363571
TI Uses of **CD4**-gamma2 and **CD4**-IgG2 **chimeras**.
AU Maddon, Paul J.; Beaudry, Gary A. (1)
CS (1) Upper Montclair, NJ USA
ASSIGNEE: Progenics Pharmaceuticals, Inc.
PI US 6187748 February 13, 2001
SO Official Gazette of the United States Patent and Trademark Office Patents,
(Feb. 13, 2001) Vol. 1243, No. 2, pp. No Pagination. e-file.
ISSN: 0098-1133.
DT Patent
LA English
AB This invention provides the **CD4**-IgG2 chimeric heterotetramer, wherein the heavy chains of the chimeric heterotetramer is encoded by the expression vector designated **CD4**-IgG2HC-pRcCMV (ATCC No. 75193). This invention also provides the **CD4**-IgG2 chimeric heterotetramer, wherein the light chains of the chimeric heterotetramer is encoded by the expression vector designated **CD4**-kLC-pRcCMV (ATCC No. 75194). This invention also provides the **CD4**-IgG2 chimeric heterotetramer, wherein the heavy chains of the chimeric heterotetramer is encoded by the expression vector designated **CD4**-IgG2HC-pRcCMV (ATCC No. 75193) and the light chains of the chimeric heterotetramer is encoded by the expression vector designated **CD4**-kLC-pRcCMV (ATCC No. 75194). Finally, this invention provides a method of inhibiting **HIV** infection of a **CD4**+ cell, a method of preventing a subject from being infected with **HIV**, and a method of treating a subject infected with **HIV** so as to block the spread of

L2 ANSWER 8 OF 100 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:522048 BIOSIS
DN PREV200100522048
TI Enhanced **HIV**-1 Gag immunogenicity by a DNA vaccine **chimera** with molecular adjuvants of the lysosomal-associated membrane protein (LAMP) and dendritic cell multi-lectin receptor (DC-MLR) in an AAV-ITR plasmid vector.
AU Lu, Y. (1); Marques, E., Jr. (1); Chikhlikar, P. R. (1); August, J. T. (1)
CS (1) Johns Hopkins School of Medicine, Baltimore, MD, 21205 USA
SO Journal of Human Virology, (May June, 2001) Vol. 4, No. 3, pp. 154. print.
Meeting Info.: 2001 International Meeting of the Institute of Human Virology Baltimore, Maryland, USA September 09-13, 2001 Institute of Human Virology
. ISSN: 1090-9508.
DT Conference
LA English
S